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The Feasibility and Utility of Continuous Sleep Monitoring in Critically Ill Patients Using a Portable Electroencephalography Monitor

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Abstract

Introduction—Sleep disruption in critically ill adults can result in acute decrements in cognitive function, including delirium, but is under-diagnosed in the setting of the intensive care unit (ICU). While sleep stages can be assessed by polysomnography (PSG), acquisition and interpretation of PSG is costly, labor intensive, difficult to do over an extended period of time with critically ill patients (multiple days of continuous recording), and may interfere with patient care. In this pilot study, we investigated the feasibility and utility of monitoring sleep in the ICU setting using a portable electroencephalography (EEG) monitor, the SedLine brain monitor.

Methods—We first performed a baseline comparison study of the SedLine brain monitor by comparing its recordings to PSG recorded in a sleep laboratory (n=3). In a separate patient cohort, we enrolled patients in the ICU who were monitored continuously with the SedLine monitor for sleep disruption (n=23). In all enrolled patients, we continuously monitored their EEG. The raw EEG was retrieved and sleep stages and arousals were analyzed by a board-certified technologist. Delirium was measured by a trained research nurse using the Confusion Assessment Method developed for the ICU.

Results—For all enrolled patients, we continuously monitored their EEGs and were able to retrieve the raw EEGs for sleep stages analysis. Overall, the SedLine brain monitor was able to differentiate sleep stages, as well as capture arousals and transitions between sleep stages when compared to the PSG performed in the sleep laboratory. The percentage agreement was 67% for the wake stage, 77% for the non-rapid eye movement (REM) stage (N1=29%, N2=88%, N3=6%) and 89% for the REM stage. The overall agreement was measured using weighted kappa, which was 0.61, 95% CI=0.58–0.64.

In the ICU study – the mean recording time for the 23 enrolled patients was 19.10 hours. There were several signs indicative of poor quality sleep, where sleep was distributed throughout the day, with reduced time spent in REM (1.38 ± 2.74 % of total sleep time), and stage N3 (2.17 ± 5.53 % of total sleep time) coupled with a high arousal index (34.63 ± 19.04 arousals/hour). The occurrence of ICU delirium was not significantly different between patients with and without sleep disruption.

Conclusion—Our results suggest the utility of a portable EEG monitor to measure different sleep stages, transitions, and arousals. However, the accuracy in measuring different sleep stages

by the SedLine monitor varies when compared with PSG. Our results also support previous findings that sleep is fragmented in critically ill patients. Further research is necessary to develop portable EEG monitors that have higher agreement with PSG.

Introduction

Sleep disruption can result in both physiological and cognitive changes. Adverse outcomes of sleep disruption include impaired immune function, which may result in increased infection and disease[1–3]; negative nitrogen balance and protein catabolism[4,5]; cardiovascular changes such as hypertension and increased sympathetic activity[6,7]; neurocognitive dysfunction such as slower reaction times and memory impairment[8,9]; and decreased quality of life measures[10]. Sleep disruption has also been proposed as one of the factors contributing to in-hospital delirium[11]. In the intensive care unit (ICU), delirium occurs in 20–80% of patients[12].

Whether the development of delirium can be reduced by interventions targeting sleep quality and quantity has not been rigorously investigated. Several small-scale studies were able to demonstrate that ICU patients have fragmented sleep due to frequent arousals and altered sleep architecture with an increase in light sleep and less slow wave and rapid eye movement (REM) sleep[13–15]. The sleep stages can be assessed by polysomnography (PSG) that includes electroencephalography (EEG)[16]. However acquisition of this type of EEG data requires polysomnographic expertise and only allows a limited period of monitoring with the need to re-apply the EEG leads for extended periods of monitoring. Specifically, standard PSG involves placement of multiple electrodes on the head, according to a mapping system, to collect a combination of EEG, eye movement and muscle tone[17]. The electrodes need continuous monitoring and maintenance, which make them unfit to be used over extended periods of time and in hospitalized patients receiving complex care. Specific patient populations such as ICU patients undergo a variety of procedures and tests throughout their stay, making it particularly difficult to maintain continuous monitoring. The removal and reapplication of electrodes may also cause skin irritation.

An alternative monitor is the actigraph, an electronic device that is a proxy for sleep by detecting a patient's movement by way of an accelerometer but this provides little insight into sleep stages, transitions and other sleep dynamics in the ICU setting[13]. Furthermore, accelerometers may not be useful in the critical care setting because lack of body motion could be less likely to represent sleep than in other settings where they appear to have utility.

Another class of brain function monitors involves the use of processed EEG which includes Bispectral index (BIS™)[18], SedLine® [19], GE Datex-Ohmeda Entropy™[20] and Narcotrend®-Compact M[21]. These monitors confer significant advantages over traditional PSG equipment because of their small size and portability, making them useful for data collection in challenging environments. These monitors also require minimal set up time and expertise resulting in potentially less interference of clinical care. While simple and easy to use, brain function monitors have been developed with the intention to improve safety and efficiency in general anesthesia. Several small studies used the BIS to monitor sleep in volunteers or patients in the hospital settings[22–24]. Processed indices, such as the ones obtained by

processed EEG, are dimensionless indices generated by proprietary algorithms from the EEG waveform. The indices do not provide any specific neurophysiological information, and numbers do not necessarily correspond to the level of consciousness or anesthetic depth. Indices might even be less informative in the setting of administration of hypnotics and/or sedative medications. A processed EEG index number can be concordant or discordant with the information conveyed by the EEG waveform[17]. Still, these portable monitors allow quick access to EEG waveforms.

The new BIS brain monitoring system provides either two channels or four channels of EEG. By measuring EEG and electromyography (EMG) signals, the GE Datex-Ohmeda Entropy monitor gives information on spectral entropy, response entropy and state entropy. The entropy module measures irregularity in spontaneous brain and facial muscular activity. The N-entropy module displays one channel of EEG. The Narcotrend-Compact M monitor provides an automatically classified EEG developed from visual classification. It has been used solely as a monitor of anesthesia depth[25].

Similar to the above monitors, the SedLine monitor uses a symmetrical bilateral array that provides four-channel data. Bifrontal electrodes measure four channels of raw EEG with separate displays for EMG, artifacts (e.g., patient motion), as well as a burst suppression ratio. The monitor uses frontal electrode placements that approximate those recommended by the American Academy of Sleep Medicine[26]. Therefore, SedLine can potentially produce sufficient EEG for recording and identification of sleep stages, which may be useful in settings that are challenging for conducting the “gold standard” PSG, such as the ICU. The capacity to directly record raw EEG (four channels) seems to be feasible for continuous monitoring in the ICU setting.

All portable brain monitors except the Narcotrend-Compact M monitor have been primarily developed to monitor the depth of sedation or anesthesia, and not to record sleep[25]. Hence, in this prospective cohort pilot study, we investigated the feasibility of monitoring sleep in the ICU setting using a portable EEG monitor, the SedLine brain monitor. The aims of this pilot study were 1) to compare the accuracy of a portable EEG monitor in measuring sleep variables in a cohort of outpatients scheduled for sleep laboratory studies who were concurrently monitored with both standard PSG and SedLine, and 2) to evaluate the feasibility of using SedLine to continuously measure the sleep-wake cycle in the ICU setting.

METHODS

This study received approval from the IRB of the University of California, San Francisco and written informed consent was obtained from all volunteer subjects and patients. The study sample size was determined using a convenient sampling technique and the study recruitment stopped when the technician trained in sleep analysis departed the research team.

Study population

Baseline comparison study—Subjects who were scheduled to have a sleep study in the sleep laboratory to exclude sleep-disordered breathing were recruited. The sleep laboratory subjects had an array of 18 PSG leads consisting of EEG, EMG, electrooculography (EOG) and respiratory monitoring. The PSG was recorded using an Embla recording System (Natus Medical Incorporated, Pleasanton, CA). The EEG data were uploaded to a Dell Optiplex 9020 computer for analysis. The raw unscored EEG was imported into RemLogic™ version 1.3 (Embla, Pleasanton, CA) and sleep stages were scored visually every 30 seconds by a certified sleep technologist blinded to the SedLine data. Typical hypnograms were generated as well as all standard sleep variables.

Simultaneous to the PSG, the subjects also had a SedLine® Brain Function Monitor (Masimo Corp., Irvine, CA) placed. The six-electrode set was applied to the patient's skin across the forehead and temporal regions to capture frontal EEG signals and EMG from the patient. Monitoring data, including sleep and wake, were continuously acquired and recorded from patients using the SedLine. Via the brain monitor, the data were collected continuously on the in-build hard disk. The brain monitor provided four channels of real-time EEG sampled at 2500 Hz. EEG signals were filtered and decimated to 250 Hz with an acquisition bandwidth of 0.5 to 70 Hz. The acquisition montage mimics electrodes placed according to the International 10–20 System – Fp1, Fp2, F7, and F8, each referenced to FpZ. In RemLogic, each EEG channel had low and high frequency filters applied (LFF 0.3 Hz, HFF 35 Hz). EEG recordings were retrieved from the in-built hard disk and uploaded to a research computer. The recordings were converted to European Data Format and were scored in 30-second epochs using RemLogic software according to the 2007 American Academy of Sleep Medicine guidelines[27].

EOG was approximated using F8-FpZ and F7-FpZ dipoles to detect right and left eye movements, respectively. These channels were filtered as EOGs, according to standard guidelines (LFF 0.3 Hz, HFF 35 Hz). Similarly, EMG was approximated from changes in forehead muscle tone in channels Fp1-F8 and Fp2-F7. These channels were filtered as EMGs (LFF 10 Hz, HFF 70 Hz). Absence of muscle tone from these leads assisted in scoring REM sleep.

ICU study—In a separate patient cohort, we enrolled 23 patients admitted to the ICU who were anticipated to remain in the ICU for at least 24 hours. In this second cohort, the inclusion criteria were patients who were English-speaking and aged 45 years or older. Exclusion criteria were: status post craniotomy; moribund state with planned withdrawal of life support; severe dementia; or substantial hearing impairment precluding delirium assessment. Electrode placement and start of monitoring took place in the first 12h after ICU admission.

SedLine Brain Monitor EEG analysis

A PSG technician who was blinded to the PSG results and to the delirium status analyzed the SedLine data. The technologist had extensive training in PSG, including the scoring of sleep, and is certified by the Board of Registered Polysomnographic Technologists.

For each patient, we calculated several sleep architecture variables at night (10 p.m. – 6 a.m.) and during their entire recording period. We measured total sleep time (TST), the proportion of time patients spent in stages 1, 2, 3 and REM and sleep efficiency (SE). SE is defined as the number of minutes of sleep divided by the number of minutes in bed, where normal is approximately 85 to 90% or higher. Sleep onset latency was measured from the time from lights out through 90 seconds of consecutive sleep. Hypnograms were used to summarize sleep architecture and describe sleep continuity among study patients. Arousals of at least 3 seconds and preceded by at least 10 seconds of sleep were marked[27]. An awakening is defined by EEG arousals lasting 15 seconds or longer. Standard definitions were used to identify sleep stages and other variables of interest in the EEG during sleep, such as spindles and slow waves.

Delirium assessment

For the critically ill patients in the second cohort, delirium was measured by a trained research nurse using the Confusion Assessment Method developed for the ICU (CAM-ICU)[28]. CAM-ICU has been well validated by multiple prior studies for use in ventilated and non-ventilated ICU patients. Sensitivity as compared to the standard of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria ranges from 81%[28] up to 100%[29] and specificity ranges from 96% to 100%[29]. The CAM-ICU is considered positive with feature 1 (acute onset of mental status change or fluctuation of mental status), feature 2 (inattention), and either feature 3 (disorganized thinking), or feature 4 (altered level of consciousness). Delirium was measured twice daily, between 8 – 10 a.m. and also between 6 – 8 p.m. by trained researchers while in the ICU. The patient was first rated on the Richmond Agitation and Sedation Scale (RASS)[30]. CAM-ICU was not administered if a patient was too sedated to be interviewed (RASS score of -4 or -5). Patients with a RASS Score of -3 or higher and a positive CAM-ICU were considered to be delirious.

Statistical analysis

Summary and descriptive statistics, including means and standard deviations, were calculated based on the results of the sleep scoring as previously described.

For assessing the utility of using SedLine to monitor sleep, the sleep staging of all epochs from PSG and from the SedLine were compared and weighted kappa statistics were used to calculate the overall agreement between the two devices. SAS version 9.4 was used for this comparison. For all aspects of the study, descriptive data were analyzed in Excel (Microsoft® Excel for Mac 2011). For comparison of the sleep variables in the patients in the ICU between those with delirium *versus* without, Mann Whitney U test was used.

RESULTS

EEG monitoring with SedLine was comparable to polysomnography

Three subjects in the sleep laboratory simultaneously monitored with PSG and SedLine provided EEG data for the baseline comparison study. While the number of subjects was small, even a small number of subjects was able to provide a very rich dataset. Among the three subjects, 2,653 epochs of sleep were scored and the agreement between the scoring

based on the recording from the gold standard PSG and the brain function monitor was compared. Overall, the recordings on the brain function monitor after sleep staging was performed off-line, capturing arousals and transitions between sleep stages, comparable to the standard PSG collected in the sleep laboratory. In particular, the SE from the Sedline tracks quite well with the PSG (Table 1). In two subjects, the sleep onset latency also showed good correlation between Sedline and PSG. The SedLine data were similar to the PSG data, and demonstrated "typical" sleep architecture, including an initial descent from lighter to deeper sleep stages at sleep onset, a concentration of deep sleep (stage N3) in the early portion of the night, a concentration of REM in the later portion of the night, and a number of transitions between sleep stages and awakenings that are within normal range[31] (Figure 1 and 2).

Overall, the percent agreement was 75%, with 77% of epochs of sleep correctly characterized as sleep. However, agreement between the two monitors varied depending on the sleep stages being evaluated (Table 2). The overall weighted kappa was 0.62, 95% CI=0.58–0.64. A higher percentage agreement was seen in the wake stage, non-REM and REM stages, and lowest for the N3 stage.

Sleep characteristics of patients in the ICU

The detailed characteristics and admitting diagnoses of the study patients are shown in Supplemental Table 1. The mean age of the patients was 68 ± 11 years. Forty-three percent of the patients were admitted for medical reasons, and the remainder were postoperative patients. During the study period, 9/23 (39%) patients received intermittent opioids for pain control, and 3/23 patients (13%) received intermittent benzodiazepines (midazolam, zolpidem or temazepam) for sedation. None of the patients received continuous sedation with opioids, benzodiazepines, propofol or dexmedetomidine (full list of medications can be found in Supplemental Table 2). Clinically, all patients had a sedation level targeted at a RASS score of 0 or -1.

In all enrolled subjects, we were able to continuously monitor and retrieve their EEG for analysis with a mean recording time for the 23 enrolled patients of 19.10 hours, suggesting that SedLine was well tolerated among our target population. A sleep report, with traditional variables, such as TST and SE was generated for the entire recording period for each patient (Supplemental Table 3). There were several signs indicative of poor quality sleep, with reduced time spent in REM (6.4 ± 12 min, 1.38 ± 2.74 % of TST, where 20–25% of TST is the normal range for this age group[32], and stage N3 (5.4 ± 11.6 min, 2.17 ± 5.53 % of TST, where 2.4–35.6% is the normal range for this age group[33,34], coupled with a high arousal index (34.63 ± 19.04 arousals/hour) where normal is 23 arousals/hour for this age group[26,35,36].

We further compared the sleep data between patients who developed delirium *versus* those who did not (Table 3). Of the 23 patients studied in this cohort, eight developed delirium (35%), as measured by a positive score on CAM-ICU. Overall, there was no statistical difference on polysomnographic variables between the two groups, although both groups had a small percentage of N3 rates and elevated arousal indices. The full results are shown in Supplemental Table 3.

DISCUSSION

A preliminary analysis to validate SedLine recordings, when compared with full PSG, indicated that the strengths of the SedLine monitor include capturing changes in the EEG, such as discerning awake from sleep when compared with data from the PSG as reflected by the SE measurements. The brain function monitor was able to capture arousals and transitions between sleep stages in patients who were monitored in the sleep laboratory, but was less accurate in determining sleep stages than in distinguishing sleep from wakefulness.

We demonstrated the feasibility of measuring sleep and wake EEG data over an extended period of time in a manner that did not interfere with the overall nursing care and management of ICU patients. In general, there was good agreement between SedLine and in-laboratory PSG for scoring all subjects. However the accuracy in measuring different sleep stages by the SedLine monitor varies, specifically, the percent agreement on N1 epochs is only 29%. It appears that when the PSG sleep stages were N1, the SedLine scores were incorrectly reported as N2 or wake. The overlap with wake might represent periods of transition when the patient is going in and out of wakefulness and, thus, the determination of which stage is dominant on a particular epoch can sometimes be difficult to assess. Similarly, slow rolling eye movements that are typically seen in N1 can appear in wakefulness as a patient is approaching N1 sleep and perhaps an overreliance on the eye movements led to misscoring with a decreased sensitivity to the alpha waves of wakefulness that are more prominent occipitally. Furthermore, both N1 and N2 have a background EEG activity described as theta waves. One of the defining features of N2 is the sleep spindle. These phenomena are more challenging to detect using solely frontal leads, as is the case with SedLine, since sleep spindles have a central-parietal peak[37]. Nonetheless, frontal leads have the benefit of good visualization of K-complexes, slow waves and eye movements. A decreased ability to detect sleep spindles may have led to poorer differentiation between N1 and N2. The lowest agreement occurs in N3 sleep stage. However, since the N3 stages count for only 3% of sleep epoches a larger sample size will be needed to further discern the reasons for misclassification for this sleep stage. Potential difficulties with this technology include the use of frontal poles as a proxy to assess EOG, and the absence of occipital leads. Using frontal poles rather than the traditionally placed EOG led to decreased accuracy in determining eye movements. Similarly, as noted above, alpha waves, which indicate the state of wakefulness, are less prominent in frontal leads so an underscoring of wake may occur. There was decreased concordance in N3 when one would have predicted the reverse, because slow waves are generally best seen in frontal leads, although our results may not be representative due to the small number of epochs or other artifacts in the signal.

Through this pilot study in the ICU, we successfully studied 23 patients, with a mean recording time of 19.10 hours, suggesting that the device was well tolerated by critically ill patients, giving insight into the sleep cycle dynamics experienced by patients in the ICU. To our knowledge, this is the first study using the SedLine monitor to measure sleep in critically ill patients.

Sleep in normal healthy adults is distributed as stage 1 – 2–5%, stage 2 – 45–55%, stage 3 – 2–36%, and REM sleep – 20–25%[32,33,35]. The stages of sleep are fragmented in ICU

patients[38,39]. Our data show trends consistent with previously published reports on sleep among ICU patients. Specifically, 1) sleep was distributed throughout the day and night rather than being consolidated at night, 2) there was a notable reduction in proportion of REM sleep, and 3) patients did not have normal sleep cycle architecture, where individuals transition from lighter to deeper sleep and alternate between non-REM and REM sleep in approximately 90 minute cycles (Figure 1).

Sleep quality and quantity in the ICU is reduced by factors that include a patient's acute illness, pain, discomfort, medical procedures, nursing-related care, ambient light, noise, mechanical ventilation, and other circadian disrupters, and medications[40,41]. Full montage EEG is generally not practical in the ICU setting and these results confirm the utility of a portable monitor to measure different sleep stages. The ease of use, comfortability, small size and portability of brain function monitors, make their use feasible for the monitoring and care of critically ill patients providing a potential use for research. Our results need further confirmation by a larger study. Although our study provided a mean recording duration of 19.10 hours, future studies should include longer duration of monitoring to capture more than one day-night cycle. However, the utility of monitoring sleep with a portable brain monitor in order to improve sleep hygiene and patient outcomes will need to be further evaluated because our pilot study did not discern any significant differences in polysomnographic variables in patients with delirium versus those without.

Summary and clinical implications

Our results confirm the feasibility of a portable EEG monitor, such as SedLine to assess sleep stages with reasonable accuracy and utility within the ICU setting. Further research should also focus on improving a processed EEG monitor that has higher agreement with PSG. Having the ability to continuously monitor sleep in the ICU setting will facilitate clinical trials with goal-directed interventions that might help understand, address and rectify sleep disruption. Targeting modifiable risk factors such as sleep disruption may ultimately decrease delirium and associated adverse events in critically ill patients, a hypothesis that remains to be tested. Specifically, tracking sleep in real-time in the clinical setting may lead to increased use of other non-pharmacologic treatments to improve sleep hygiene such as the use of earplugs, eyeshades, noise reduction and others.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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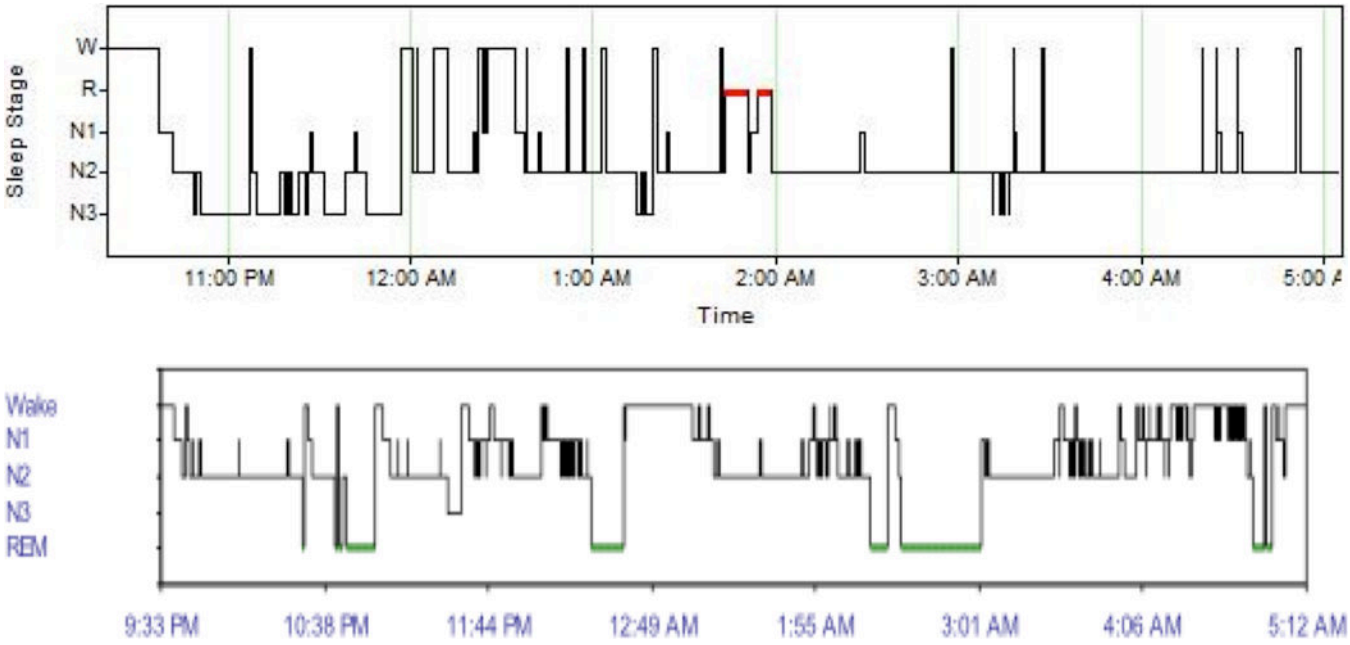

Figure 1.

Hypnogram generated from an individual who was in the sleep laboratory.

A) Hypnogram generated using SedLine recording

B) Hypnogram generated from polysomnography recording

R=rapid eye movement; N1=non-REM stage 1; N2=non-REM stage 2; N3=non-REM stage 3.

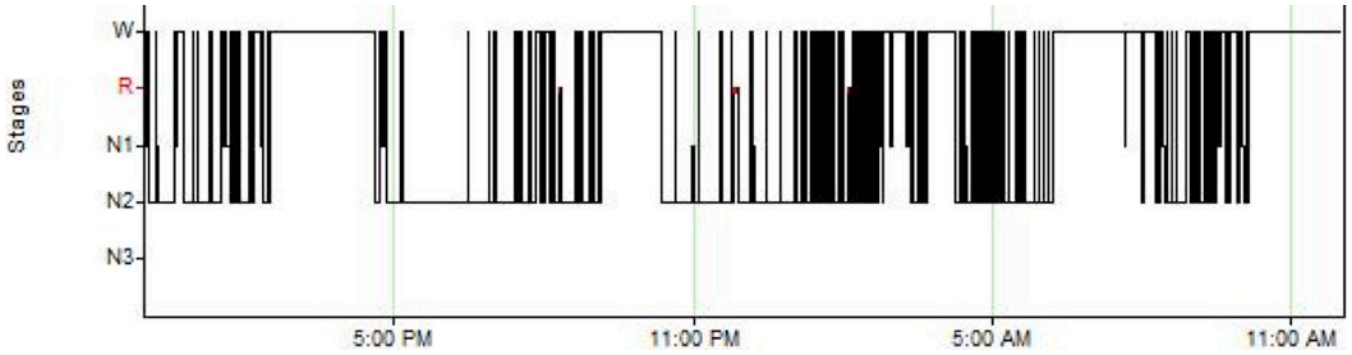

Figure 2.

Hypnogram generated from the SedLine recording of one critically ill patient demonstrating frequent transitions between sleep and wake during both the day and night.

R=rapid eye movement; N1=non-REM stage 1; N2=non-REM stage 2; N3=non-REM stage 3.

Table 1

Sleep onset latency and sleep efficiency comparison between SedLine and polysomnography in subjects presenting to the sleep laboratory

A) Sleep onset latency (a sleep onset latency of >20 minutes is typically considered prolonged)		
	PSG (min)	**SedLine (min)**
Subject 1	20	29
Subject 2	1.5	13
Subject 3	27.5	28.5

B) Sleep efficiency (percent of time spent asleep/total time from lights out to lights on)		
	PSG	**SedLine**
Subject 1	83%	80%
Subject 2	93%	91%
Subject 3	77%	80%

PSG=polysomnography; min=minutes.

Table 2
Comparison between polysomnography and SedLine monitor

Percent agreement between scorings of the PSG *versus* SedLine by sleep stage. The overall weighted kappa was 0.62.

Sleep stage	Percentage agreement with PSG
Wake (n= 421)	67
Non-REM	
N1 (n= 340)	29
N2 (n= 1639)	88
N3 (n= 77)	6
REM (n= 176)	89

PSG=polysomnography; REM=rapid eye movement; N1=drowsy sleep: slow rolling eye movements with brain waves in the 5 to 7 Hz range; N2=light sleep:eye *movements stop and there are occasional short bursts of rapid waves called* sleep spindles (11–16 Hz) and characteristic negative sharp waves followed by a positive component called K-complexes; N3= deep sleep: *extremely slow brain waves called* delta waves (0.5 to 2 Hz with minimum amplitude of more than 75 microV) begin to appear and comprise at least 20% of the 30-second epoch; n=number of sleep epochs analyzed for each stage.

Table 3

Sleep report of all 23 enrolled patients in Intensive Care Unit.

	Overall	CAM (+) n = 8	CAM (−) n = 15
Sleep Statistic			
Recording time (min)	1145.9 (873.37)	1322.29 (1318.71)	1068.69 (634.24)
Wake during the recording period (min)	716.80 (575.61)	748.79 (768.53)	702.81 (499.00)
TST (min)	364.46 (402.55)	483.50 (613.31)	312.38 (278.75)
Durations			
REM (min)	6.4 (12.0)	3.1 (3.4)	7.8 (14.2)
REM % of TST	1.4% (2.7)	0.8% (1.1)	1.6% (3.2)
N1 (min)	119.9 (160.8)	195.0 (270.3)	87.1 (70.1)
N1 % of TST	33.1% (22.8)	28.4% (23.0)	35.1% (23.1)
N2 (min)	232. (268.2)	273.8 (349.4)	214.8 (235.6)
N2 % of TST	67.7% (28.6)	80.1% (20.41)	62.3% (21.1)
N3 (min)	5.4 (11.6)	11.6 (16.0)	2.6 (8.3)
N3 % of TST	2.2% (5.5)	5.0% (8.2)	1.0% (3.5)
Transition rate (per hr)	12.2 (8.5)	13.7 (8.4)	11.6 (8.7)
Arousal rate (per hr)	34.6 (19.0)	33.6 (13.4)	35.1 (21.4)

Data are presented as mean value (±SD).

CAM=confusion assessment method; REM=rapid eye movement; N=non-rapid eye movement; TST=total sleep time.